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10/541,020	06/28/2005	Kenji Fujii	Q88147	4034

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/11/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/541,020	FUJII ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds Draper	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2010 and 15 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28 and 38-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 28 and 38-39 are presented for examination.

Applicant's Amendment filed July 26, 2010 was received and entered into the present application. Pursuant to the notice dated October 14, 2010, the reply filed July 26, 2010 was non-compliant. Applicant's subsequent submission dated November 15, 2010 has been received and entered into the present application.

Due to the acceptable nature of the Terminal Disclaimer filed November 15, 2010, the obviousness-type double patenting rejection over U.S. Patent Application No. 11/993,743 is withdrawn.

Claims 28 and 38-39 remain pending and under examination. Claims 29-30 and 37 are cancelled. Claims 28 and 39 are amended.

Applicant's arguments, filed July 26, 2010 and November 15, 2010, have been carefully considered. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 103

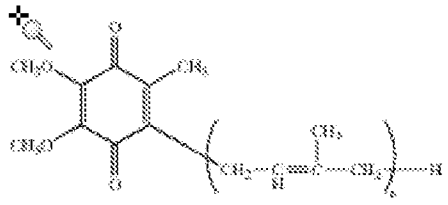
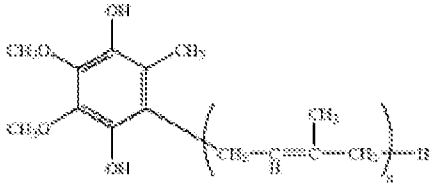
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujii et al. (WO 2002/092067; 2002), citing to U.S. Patent Application Publication No. 2004/0115181 (2004) for an English translation, in view of Wilson et al. ("Exertional Fatigue Due to Skeletal Muscle Dysfunction in Patients with Heart Failure", Circulation, 1993; 87:470-475), further in view of Remington's Pharmaceutical Sciences (Fifteenth Edition, 1980; p.712), each already of record, for the reasons of record set forth at p.5-12 of the previous Office Action dated March 25, 2010, of which said reasons are herein incorporated by reference.

Newly amended claims 28 and 39 remain properly included in the present rejection because Fujii et al. teaches a composition for transmucosal administration comprising an oxidized coenzyme Q of the formula  , wherein n represents an integer of 1 to 12, and/or reduced coenzyme Q of the formula  , wherein n also represents an integer or 1 to 12 (p.1, para.[0007-0009]), wherein coenzyme Q with 10 side chain repeating units (i.e., an oxidized coenzyme Q10 and reduced coenzyme Q10) are preferably used (p.2, para.[0016]), wherein the total content of the above oxidized and reduced coenzyme Q amounts to 0.0001-99% by weight of the

total composition (p.1, para.[0010]). Fujii et al. further teaches a method for treating, inter alia, cerebral infarction, heart failure, etc. (p.2, para.[0023]) comprising applying the composition for transmucosal administration to human or animal mucosa with a disease (p.5, col.18), such as, inter alia, to the oral mucosa (i.e., "orally" as in instant claim 38; p.1, para.[0011]), using, for example, an oral mucosal applicator, toothpaste or drop (p.2, para.[0019]), wherein the composition may be used in humans, including aged persons (p.4, para.[0042]), dogs, cats, race horses, cows, horses, pigs, rabbits, rats, mice, birds and the like (p.1, para.[0010]).

The teachings of wherein the total content of the above oxidized and reduced coenzyme Q amounts to 0.0001-99% by weight of the total composition (i.e., which is understood to mean that each of the oxidized and reduced coenzyme Q components can be present in an amount of 0.001-99% by weight of the total composition; p.1, para.[0010]) by Fujii et al. renders the presently claimed range of (1) the ratio of reduced coenzyme Q to the total coenzyme Q to be not less than 80% by weight (claim 28) or (2) the ratio of reduced coenzyme Q to the total coenzyme Q to be 80-99.5% by weight (claim 39) prima facie obvious to one of ordinary skill in the art at the time of the invention. In particular, an express teaching that each of the oxidized or reduced coenzyme Q components are present in an amount of 0.0001-99% by weight of the total composition clearly overlaps with those ranges specifically recited in the present claims. As stated in the MPEP at §2144.05, "In the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)…"[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). See also In re Harris, 409 F.3d 1339, 74 USPQ2d 1951 (Fed. Cir. 2005)."

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the reduced coenzyme Q employed in Ex.1 and 2 contained 1% oxidized coenzyme Q (p.17, l.11-12 of the specification) and, thus, contrary to the Examiner's position, the examples did employ a combination of reduced coenzyme Q and oxidized coenzyme Q. Applicant states that the instant claims are now limited to reduced coenzyme Q_{10} and oxidized coenzyme Q_{10} or to 100% reduced coenzyme Q_{10}, of which the unexpected results shown in Ex.4 regarding use of 99% reduced coenzyme Q_{10} supports unexpected results for 100% reduced coenzyme Q_{10}. Applicant further opines that the instant claims are also limited to the ratio of reduced coenzyme Q_{10} to total coenzyme Q_{10} to be not less than 80% and that the unexpected results shown using the "exemplified ratio would have been expected to occur over the ratio range set forth in the amended claim 28" (p.8, Remarks).

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, Applicant's statement that the reduced coenzyme Q employed in Ex.1 and 2 contained 1% oxidized coenzyme Q (p.17, l.11-12 of the specification) and, thus, contrary to the Examiner's position, the examples did employ a combination of reduced coenzyme Q and oxidized coenzyme Q is noted. Examples 1 and 2 and Comparative Examples 1 and 2 are directed to the levels of coenzyme Q in the muscle following administration of reduced coenzyme Q_{10} (which contained about 1% of oxidized coenzyme Q_{10}) or oxidized coenzyme Q_{10} as compared to the control group, wherein the level of coenzyme Q was predicted to increase the energy supply to the muscle via its effects on the ATP-generating system such that it is possible to provide an anti-fatigue effect when coenzyme Q levels are elevated. Tables 1 and 2 demonstrated that the levels of coenzyme Q were elevated in muscle following administration of the reduced coenzyme Q_{10} formulation (i.e., reduced coenzyme Q_{10} plus 1% oxidized coenzyme Q_{10}). See p.19-20 of the instant specification. However, while such results as demonstrated in Tables 1-2 of the instant specification may very well establish an unexpectedly greater elevation of

coenzyme Q in muscle as compared to the control and/or oxidized coenzyme Q_{10} groups (see, again, Tables 1-2, p.19-20), the results fail to establish an unexpected effect commensurate in scope with the instant claims because the unexpected effect(s) is limited to a single combination of reduced coenzyme Q_{10} plus 1% oxidized coenzyme Q_{10}, whereas the instant claims are directed to the use of any combination of reduced coenzyme Q_{10} to total coenzyme Q_{10} in a ratio of 60-100% by weight, which clearly circumscribes a significant number of embodiments for which no unexpected effect has been demonstrated.

Secondly, as previously explained to Applicant, with regard to the data provided in Ex.3, Comparative Ex.3, Ex.4 and Comparative Ex.4, the data again fails to be commensurate in scope with the instantly claimed subject matter. In particular, the results of Ex.4 and Comparative Ex.4 (by Applicant's own admission at p.5 of the Remarks filed January 20, 2010), the results of Ex.3 were not relied upon by Applicant to demonstrate an unexpected result) are restricted to the use of either (a) reduced coenzyme Q_{10} with 1% oxidized coenzyme Q_{10} (which is understood to circumscribe a formulation comprising reduced coenzyme Q_{10} in 99% by weight with 1% by weight oxidized coenzyme Q_{10} or (b) oxidized coenzyme Q_{10} on aged rats to determine the effect on maximum running time. Though it is noted that a statistically significant increase was demonstrated on maximum running time in aged rats treated with the 300 mg/kg reduced coenzyme Q_{10} + 1% oxidized coenzyme Q_{10} combination in soybean oil (see, e.g., Table 4 at p.22 of the instant specification) as compared to the control group (which received soybean oil alone) or the 300 mg/kg oxidized coenzyme Q_{10} group, the instant claims are directed to the use of a combination of reduced coenzyme Q_{10} with oxidized coenzyme Q_{10} wherein the ratio of reduced coenzyme Q_{10} to total coenzyme Q_{10} ranges from 60-100% by weight.

These proffered results, however, do not provide a basis for concluding that the full scope of the claimed subject matter would not have been obvious because the results are limited to a very specific combination (i.e., 300 mg/kg reduced coenzyme Q_{10} + 1% oxidized coenzyme Q_{10} in soybean oil), while

the instant claims subject to this rejection encompass the use of the combination of a reduced coenzyme Q_{10} with oxidized coenzyme Q_{10}, wherein the amount of reduced coenzyme Q to the total amount of coenzyme Q ranges from 60-100% by weight. Further, it has not been demonstrated on the record that the results obtained with the exemplified combination(s) of reduced coenzyme Q_{10} in an amount of 300 mg/kg with 1% oxidized coenzyme Q_{10} in soybean oil would have been exemplary of the same or substantially similar results that would have been expected to occur over the wide range of therapeutic amounts of each of the reduced and/or oxidized coenzyme Q components of the claimed agent (i.e., that the reduced coenzyme Q_{10} component may be used in an amount of 60-100% by weight of the total coenzyme Q in the formulation). This is further exacerbated by the fact that Applicant has proffered the results of a single formulation (reduced coenzyme Q_{10} in an amount of 300 mg/kg with 1% oxidized coenzyme Q_{10}, which is interpreted as meeting a formulation comprising reduced and oxidized coenzyme Q_{10} wherein the reduced coenzyme Q_{10} is 99% by weight of the formulation and the oxidized coenzyme Q_{10} is 1% by weight of the formulation, such that the ratio of reduced coenzyme Q_{10} to total coenzyme Q_{10} is 99% by weight) as evidence of an unexpected effect, but fails to provide any other formulations with varying ratios such that, at minimum, a trend that could reasonably be extended to circumscribe a range of amounts that would provide this same unexpected effect.

In this regard, MPEP §2144.08(II)(B) is relied upon and reads, in-part: "When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the Applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition. See, e.g., In re Chupp, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a prima facie case of obviousness. Id. For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a prima facie case of

obviousness if a skilled artisan 'could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof.' In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (**Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.**) But see, In re Grasselli, 713 F.2d at 743, 218 USPQ at 778 (Evidence of superior properties for sodium containing composition insufficient to establish the non-obviousness of broad claims for a catalyst with 'an alkali metal' where it was well known in the catalyst art that different alkali metals were not interchangeable and Applicant had shown unexpected results only for sodium containing materials); In re Greenfield, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978) (Evidence of superior properties in one species insufficient to establish the nonobviousness of a subgenus containing hundreds of compounds); In re Lindner, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) (one test not sufficient where there was no adequate basis for concluding the other claimed compounds would behave the same way)." (emphasis added)

Here, even though the results shown with the 300 mg/kg reduced coenzyme Q_{10} plus 1% oxidized coenzyme Q_{10} in soybean oil formulation demonstrated a statistically significant effect in prolonging maximum running time (i.e., reducing fatigue) in aged rats treated with the formulation that appears to be both unexpected and unpredictable from the prior art, just as a single point in space fails to define a line, the results demonstrated for this discrete combination is insufficient to establish the non-obviousness of the entirety of the presently claimed subject matter [i.e., reduced coenzyme Q_{10} in combination with oxidized coenzyme Q_{10} in amounts wherein the ratio of reduced coenzyme Q to total coenzyme Q ranges from 60-100% by weight] absent any concrete evidence or scientifically sound reasoning as to why any other amounts of the claimed reduced and/or oxidized coenzyme Q would have been reasonably expected to demonstrate the same apparently unexpected effect in reducing fatigue in an aged animal.

Applicant, however, attempts to remedy this lack of evidence and/or sound reasoning by arguing that the unexpected results shown using the "exemplified ratio would have been expected to occur over the ratio range set forth in the amended claim 28" (p.8, Remarks). This is most certainly found to be unpersuasive. The admission that a purportedly unexpected result would have been expected to be observed over the range of amounts instantly claimed is clear evidence, provided by Applicant, that the effect is, in fact, not at all unexpected. An expectation of an allegedly "unexpected result" does not then make it unexpected, if one of skill in the art at the time of the invention would have expected it to occur. Thus, Applicant appears to have admitted on the record that the unexpected results alleged to occur over the entire claimed range are actually not unexpected, but rather would have been expected by the skilled artisan and, as a result, fail to amount to an "unexpected result" that would be a secondary consideration probative of nonobviousness (aside, of course, from the single data point for which Applicant has provided supporting evidence of an unexpected effect as discussed supra).

Applicant is again reminded that, should he rely upon unexpected results to patentably distinguish over the prior art, the present claimed must be limited to the embodiment(s) which is (are), in fact, unexpected. Note also that Applicant is burdened with the responsibility of explaining why the evidence provided to support secondary considerations is probative of non-obviousness beyond what data is explicitly provided as unexpected. Please see MPEP §716.02(b)[R-2], particularly Section (II), which states, "[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness." Ex parte Ishizaka, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992). In the instant case, though the instant data was provided in the instant specification and not a declaration, the burden is nonetheless on Applicant to explain the data provided as evidence of non-obviousness of the claimed subject matter.

In view of the reasons provided supra, the evidence supporting the obviousness of the instantly claimed invention outweighs the remarks and evidence provided to support the non-obviousness of the

instantly claimed invention. Therefore, the rejection stands.

For these reasons supra, and those previously made of record at p.5-12 of the Office Action dated March 25, 2010, rejection of claims 28 and 38-39 is proper.

Conclusion

Rejection of claims 28 and 38-39 is proper.

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds Draper whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds Draper/
Primary Examiner, Art Unit 1614

February 7, 2011